IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

ABBOTT GMBH & CO., KG, ABBOTT BIORESEARCH CENTER, INC., ABBOTT BIOTECHNOLOGY, LTD. Plaintiffs, v. CENTOCOR ORTHO BIOTECH, INC., CENTOCOR BIOLOGICS, LLC. Defendant.	C.A. No. 4:09-CV-11340 (FDS) JURY TRIAL DEMANDED **PUBLICLY REDACTED VERSION**

ABBOTT'S REBUTTAL CLAIM CONSTRUCTION BRIEF REGARDING THE TERM "HUMAN ANTIBODY"

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I. INTRODUCTION

Abbott respectfully requests leave to file this rebuttal to Centocor's Supplemental Claim Construction Brief ("Centocor's Supplemental Brief" or "Centocor Suppl. Br."), filed on March 28, 2011.[1] Centocor's Supplemental Brief asserts new claim construction arguments, made for the first time in their March 28, 2011 filing. Centocor has proposed a construction of the term "human antibody" that has no basis in the law and excludes certain preferred embodiments disclosed in the specification. Abbott believes this rebuttal is necessary to address these new arguments.

II. CENTOCOR'S CLAIM CONSTRUCTION ANALYSIS IS FLAWED AS A LEGAL MATTER

The claim construction standards Centocor urges this Court to apply are not based in the law and should, therefore, be disregarded.

A. A Proper Claim Construction Analysis Focuses on the Meaning of the Term to a Person of Ordinary Skill in the Art at the Time of the Invention

The Federal Circuit has made clear that a claim term should be construed based on its "ordinary and customary meaning," defined as "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). In those cases where the ordinary meaning of a claim term as understood by a person of skill in the art ("POSA") is readily apparent even to lay persons, the ordinary meaning becomes the acquired meaning of the term. *Id.* at 1314. In many cases, however, "determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art." *Id.* In such cases, the Court looks to "those sources

[1] A redacted version of Centocor's Supplemental Brief was filed on March 28, 2011, at Docket Entry No. 144; a full version of this brief was filed under seal on March 29, 2011, at Docket Entry No. 146.

available to the public that show what a person of skill in the art would have understood disputed claim language to mean." *Id.* Those sources consist of, as a preliminary matter, intrinsic evidence – "the words of the claims themselves, the remainder of the specification, the prosecution history," and, as a secondary matter, "extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* at 1314 (internal quotations and citations omitted), 1315-17.

B. Centocor's Assessments of Practicality, Clarity, and Intent Are Irrelevant in a Claim Construction Analysis

Contrary to claim construction law, Centocor argues that its proposed claim construction should be accepted over Abbott's because it "provides a practical definition" whereas Abbott's construction purportedly "does not provide meaningful clarity" in defining 'human antibody' by "how it is made" rather than "by the antibody's structure." (Centocor Suppl. Br. at 9; *see also id.* at 1, 13.) Centocor seems to confuse written description requirements under 35 U.S.C. § 112 with standards applied in a claim construction analysis. In fact, the law does not prohibit construing terms based on how something is made; moreover, there is no requirement of "practicality" or "meaningful clarity" in a claim construction analysis. *See Phillips*, 415 F.3d at 1312-19.

In any event, Centocor's assertion that the phrase "derived from human DNA" in Abbott's proposed construction is not clear (Centocor Suppl. Br. at 9) is factually incorrect because a POSA would understand that if DNA is taken from a human source, it is derived from human DNA.[2] A POSA would understand that if an antibody is obtained from a phage library

[2] Centocor's position is particularly perplexing because in the litigation *Centocor, Inc., et al. v. Abbott Laboratories, et al.*, Civil Action No. 2:07cv139 (TJW), Centocor advanced and the Court adopted [redacted] (*See* Gunther Apr. 12 Decl. Ex. 22, [Centocor's] Opening Claim Construction Br. in *Centocor, Inc., et al. v. Abbott Laboratories, et al.*, Civil Action No. 2:07cv139, at 18-19.)

made from human-sourced DNA, that antibody would be encompassed within the construction of human antibody proposed by Abbott.

This understanding is further supported by the specification, which states that "the term 'human antibody,' as used herein, is not intended to include antibodies in which CDR sequences [are] *derived* from the germline of another mammalian species . . . ." (Pearson Mar. 28 Decl.[3] Ex. 2, '128 Patent at col.27 ll.10-14 (emphasis added).) It is also supported by the prosecution history of the '485 Patent, which shows that the patent claims were amended in 2008 to recite the term "human antibody" in order to distinguish the patent claims from three cited references that discussed antibodies derived from mice, rats, and rabbits. (Gunther Apr. 12 Decl.[4] Ex. 23, Amendment and Response to Office Action, dated Dec. 4, 2007 at 2, 4, 16-20.) This intrinsic evidence emphasizes that the PTO and the inventors understood that what makes Abbott's antibody "human" is its derivation from human DNA, as opposed to the DNA of other species. *See Phillips*, 415 F.3d at 1317 (explaining that courts should consider the prosecution history in a claim construction analysis because, like the specification, it is intrinsic evidence that shows "how the PTO and the inventor understood the patent"). This understanding is, likewise, consistent with how Brent Iverson, Abbott's expert in the interference proceeding initiated by Centocor in December 2007, understood the term "human antibody" to be used in the '128 Patent. (Gunther Mar. 7 Decl.[5] Ex. 15, Iverson Tr. at 63:9-15 ("I believe the term 'human

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[3] "Pearson Mar. 28 Decl." refers to the Declaration of Mathew A. Pearson in Support of Defendants' Supplemental Claim Construction Brief, filed by Centocor on March 28, 2011, at Docket Entry No. 142.

[4] "Gunther Apr. 12 Decl." refers to the Declaration of Robert J. Gunther, Jr. in Support of Abbott's Rebuttal Claim Construction Brief Regarding the Term "Human Antibody," filed contemporaneously with this brief on April 12, 2011, as Exhibit B to Abbott's Motion for Leave to File Abbott's Rebuttal Claim Construction Brief Regarding the Term "Human Antibody."

[5] "Gunther Mar. 7 Decl." refers to the Declaration of Robert J. Gunther, Jr. in Support of Abbott's Opposition to Centocor's Motion to Amend Claim Construction Pleadings, filed on March 7, 2011, at Docket Entry No. 131.

antibody' refers to an antibody that is derived from a human . . . . This is distinct from sequences derived from antibodies . . . from other species that have been grafted in.").)

Additionally, Centocor improperly focuses on the supposed intent of the inventors in listing the 1991 Kabat reference, as opposed to the Vbase database, in the specification to which Centocor points for its proposed claim construction. (Centocor Suppl. Br. at 10, 12.) However, the inventors' purported intentions in this context are not relevant to a claim construction analysis. While an inventor's intention is dispositive if the specification or file history reveals "an intentional disclaimer, or disavowal, of claim scope by the inventor," *Phillips*, 415 F.3d at 1316, that is not the case here. Therefore, as with Centocor's consideration of practicality and clarity, Centocor's characterization of the intentions of the inventors is irrelevant to this Court's construction of the term "human antibody."[6]

III. CENTOCOR'S PROPOSED CONSTRUCTION IS INCONSISTENT WITH THE SPECIFICATION

Centocor's proposed construction for the term "human antibody" is inconsistent with the language of the specification and improperly excludes certain preferred embodiments disclosed therein.

A. The Inclusionary Nature of the First Portion of the Specification Passage at Issue Is Underscored by the Exclusionary Nature of Its Second Portion

The particular specification passage discussing the term 'human antibody' has two parts – one inclusionary and one exclusionary – that contrast each other and point to the flaw of Centocor's argument. The first, inclusionary portion follows the word "includes" and gives exemplary descriptions of the types of antibodies the term 'human antibody' can encompass.

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[6] Centocor also inappropriately uses the claim construction process to make arguments regarding patentability under 35 U.S.C. § 103, which this Court should disregard. (*See* Centocor Suppl. Br. at 4 (stating that methods for screening a phage display library for antibodies that bind to IL-12 "were known in the art" (internal quotations and citation omitted)); *id.* at 5 (referring to site-directed mutagenesis as a "known process" involving a "standard set of procedures").)

('128 Patent, col.26 l.55 - col.27 l.10.) The second portion, however, gives one requirement of what the term excludes: "antibodies in which CDR sequences derived from the germline ***of another mammalian species, such as a mouse***, have been grafted onto human framework sequences." (*Id.* at col.27 ll.10-14 (emphasis added).) A contextual reading of the full passage, therefore, supports the understanding that the embodiments listed as inclusions in the first part of the passage are exemplary and not exhaustive, as the plain meaning of "includes" conveys, while the second part of the passage lists an exclusion that is closed and prevents the term "human antibody" from taking on the characteristics of "another mammalian species" as outlined in the exclusion listed.

B. Contrary to Centocor's Argument, "Can Have" Does Not Mean "Must Have"

Centocor misconstrues the sentence "[t]he human antibody *can have up to* twenty positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence" as meaning that the human antibody *must have* no more than twenty positions that can be different from human germline sequences. (Centocor Suppl. Br. at 8 (quoting col.27 ll.4-6 (emphasis added).) However, a reading of this sentence in the context of the sentences that precede and follow it reveals the flaw of Centocor's argument.

The preceding sentence states: "The human antibody *can have at least* one position replaced with an amino acid residue, e.g., an activity enhancing amino acid residue which is not encoded by the human germline immunoglobulin sequence." ('128 Patent at col.26 l.27 - col.27 l.4 (emphasis added).) According to Centocor's logic, the use of the phrase "can have" in this sentence would require a human antibody to have at least one position replaced with an amino acid residue. However, such an interpretation would mean that a human antibody cannot be 100% human germline. This would not make sense, as there is no reason why a human antibody

cannot completely coincide with human germline and still be considered a human antibody.

The sentence that follows states: "In other embodiments, up to ten, up to five, up to three or up to two positions are replaced." (*Id.* at col.27 ll.6-8.) It is clear from this sentence that what the passage as a whole is referring to are different embodiments that *can*, but need not, have various positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence. However, it is not stating that these various embodiments *must have* no more than twenty, ten, five, three, or two positions replaced. Nor is it stating, as Centocor proposes, that there is any kind of bright line as to what specific number of changes from human germline render an antibody derived from human DNA no longer human. Indeed, it would be improper to read these references to different embodiments as claim limitations. *See, e.g.*, *JVW Enterprises, Inc. v. Interact Accessories, Inc.*, 424 F.3d 1324, 1335 (Fed. Cir. 2005); *Phillips*, 415 F.3d at 1323.

C. Certain Preferred Embodiments Are Not in Kabat (1991), Which Shows That the Reference is Exemplary And Not Definitional

Centocor's attempt to limit the term "human antibody" to the confines of the 1991 Kabat book improperly excludes certain preferred embodiments, discounts the specification's parallel references to the Vbase database, and disregards the fact that such databases are tools, not discoveries.

A construction of the term "human antibody" that is tied to only those sequences listed in the Kabat 1991 book improperly excludes certain preferred embodiments disclosed in the patents because their closest corresponding sequences are *not* listed in Kabat (1991). Figure 1 of the specification shows that the inventors identified "Cos 3" (in figures 1A and 1B) and "DPL8" (in figures 1C and 1D) as sequences most similar to certain preferred antibody embodiments disclosed in the patents. However, a review of the Kabat 1991 book reveals that these sequences

are not listed among the sequences published in the 1991 version of that book. Therefore, it would be incorrect to adopt Centocor's construction requiring a strict comparison only to germline sequences listed in the Kabat 1991 book, because it would result in the exclusion of preferred embodiments, and such a result is "rarely, if ever, correct." *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276-77 (Fed. Cir. 2008) (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583-84 (Fed. Cir. 1996)).

Notably, "Cos 3" and "DPL8" *are* found in the Vbase database, a sequencing database confirmed in the specification as used by the inventors leading up to and at the time of the filing. (*See* '128 Patent at fig. 1, col.23 l.58-col.24 l.5, col.25 ll.56-59, col.41 ll.1-8, col.41 l.65-col.42 l.2, col.44 ll.44-47, col.44 l.63-col.45 l.2, appendix A, table 1, col.104 ll.33-38; Gunther Apr. 12 Decl. Ex. 24, Vbase database sequence excerpts, at 3, 11.) This makes sense because, at the time of the invention, a POSA would not understand the definition of human antibody to be locked into a decade-old database, as Centocor proposes. Indeed, while Centocor focuses on the potential expansion of the patent claims "after the filing date because of additional known, human sequences being added to a database" (Centocor Suppl. Br. at 11), it ignores the fact that known germline sequences were added to sequencing databases, including the Kabat and Vbase databases, between 1991 and 1999, when the patent application was filed. (*See* Gunther Mar. 7 Decl. Ex. 12 Johnson and Wu, *Kabat Database and Its Applications: 30 Years After the First Variability Plot*, 28 NUCLEIC ACIDS RESEARCH, No. 1, 2000 at 214 ("Massive amounts of sequence data are being continuously published in the scientific literature . . . We have previously published five editions of these sequences . . . In 1991, the fifth edition (2) consisted of three volumes. Currently, the database is more than five times as large."); http://vbase.mrc-

cpe.cam.ac.uk.) Centocor's attempt to limit the construction of "human antibody" to sequences as of a ***1991*** date, eight years prior to Abbott's 1999 filing date, is improper.

Additionally, Centocor's argument that sequences added to these databases after the filing date could conceivably expand the scope of the patent claims "to cover new discoveries" (Centocor Suppl. Br. at 11 (citing *Philips*, 415 F.3d at 1313; *Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1353-54 (Fed. Cir. 2000)) is unsound as a matter of fact and law. In fact, the universe of human sequences is not expanding; it is just that the tools, or databases, used to compare exact sequences and to determine if a sequence was derived from human DNA consistently get better and more accurate. (*See, e.g.*, Gunther Mar. 7 Decl. Ex. 12; http://vbase.mrc-cpe.cam.ac.uk.) It would, therefore, make sense that scientists, whether today or in 1999, would look to the best tool available, and potentially to multiple tools, to do this comparison.

IV. CENTOCOR'S ATTEMPT TO RELY ON EXTRINSIC INVENTOR TESTIMONY IS NOT PERSUASIVE

Centocor's reliance on the work of inventor Michael White (Centocor Suppl. Br. at 11-12) does not support its claim construction position.

As Centocor itself concedes, evidence of Mr. White's work "is not evidence intrinsic to the patent" and, therefore, not entitled to significant weight as a matter of law. (Centocor Suppl. Br. at 12.) *See also JVW Enterprises*, 424 F.3d at 1335; *Phillips*, 415 F.3d at 1323 (cautioning against limiting claim construction to an embodiment). If anything, Mr. White's testimony contradicts Centocor's position that the term "human antibody" is limited to twenty positions replaced with amino acid residues because Mr. White confirmed that [redacted]

(Gunther Apr. 12 Decl. Ex. 25, White Tr. at 84:5-15.) Mr. White also testified that [redacted]

[redacted]. (*Id.* at 80:1-14.) This contradicts Centocor's point that Mr. White relied on the Kabat 1991 book in his sequencing work.

V. CONCLUSION

For the reasons set forth herein, in Abbott's Supplemental Claim Construction Brief Regarding the Term "Human Antibody," and in Abbott's Opposition to Centocor's Motion to Amend Claim Construction Pleadings, Abbott respectfully requests that the Court construe the term "human antibody" to mean "an antibody that is derived from human DNA and not from the DNA of any non-human species."

Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that, on April 12, 2011, this document (filed through the ECF system) will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF).

/s/ Robert J. Gunther, Jr.